



(11) **EP 1 584 334 A3**

(12) **EUROPEAN PATENT APPLICATION**

(88) Date of publication A3:
04.10.2006 Bulletin 2006/40

(51) Int Cl.:
A61K 31/221 ^(2006.01) **A61P 11/00** ^(2006.01)
A61P 11/06 ^(2006.01) **G01N 30/00** ^(2006.01)
G01N 33/00 ^(2006.01)

(43) Date of publication A2:
12.10.2005 Bulletin 2005/41

(21) Application number: **04255015.2**

(22) Date of filing: **20.08.2004**

(84) Designated Contracting States:
AT BE BG CH CY CZ DE DK EE ES FI FR GB GR
HU IE IT LI LU MC NL PL PT RO SE SI SK TR
Designated Extension States:
AL HR LT LV MK

(72) Inventor: **Truong, Van Hung**
Westerville
Ohio 43082 (US)

(30) Priority: **01.04.2004 CA 2463001**

(74) Representative: **Bentham, Andrew**
J.A. Kemp & Co.
14 South Square
Gray's Inn
London WC1R 5JJ (GB)

(71) Applicant: **Methapharm Inc.**
Brantford,
Ontario N3T 2V6 (CA)

(54) **Solution based methacholine formulations**

(57) The present invention provides inhalable solution based formulations of methacholine that are stable, sterile and ready-to-use. Also provided are methods for preparing the ready-to-use methacholine formulations.

The formulations are useful in methacholine challenge testing for assessment of airway hyper-responsiveness in a subject.

EP 1 584 334 A3



European Patent
Office

EUROPEAN SEARCH REPORT

Application Number
EP 04 25 5015

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
X	WATSON, B.L., CORMIER, R.A. AND HARBECK, R.J.: "Effect of pH on the stability of methacholine chloride in solution" RESPIRATORY MEDICINE, vol. 92, March 1998 (1998-03), pages 588-592, XP009048090 the whole article, particularly page 589, left-hand column, line 12 to right-hand column, line 15, table 1, discussion	1-6, 12, 22-24	A61K31/221 A61P11/00 A61P11/06 G01N30/00 G01N33/00
X	BONTE, F. ET AL.: "Contribution pharmaceutique à l'exploration de l'hyperréactivité bronchique non spécifique" ANN PHARM FR, vol. 58, 2000, pages 165-169, XP009048091 * page 166, right-hand column, line 4 - page 167, right-hand column, line 3; figure 3 *	1-3, 7, 9, 12-14, 22-24	
Y	ACAR, V. ET AL.: "Stability of stored methacholine solutions: study of hydrolysis kinetic by IP-LC" JOURNAL OF PHARMACEUTICAL AND BIOMEDICAL ANALYSIS, vol. 25, July 2001 (2001-07), pages 861-869, XP001206335 * page 868, left-hand column, line 37 - page 869, left-hand column, line 3 *	1, 12, 22-24	TECHNICAL FIELDS SEARCHED (Int.Cl.7) A61K G01N
Y	RUBINFELD, A.R. & PAIN, M.C.F.: "Perception of asthma" LANCET, vol. 7965, 24 April 1976 (1976-04-24), pages 882-884, XP009048032 * page 883, right-hand column, lines 1-25 *	1, 12, 22-24	
----- -/--			
The present search report has been drawn up for all claims			
Place of search Munich		Date of completion of the search 30 August 2005	Examiner Venturini, F
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	

5
EPO FORM 1503 (03.02) (P04001)



European Patent
Office

EUROPEAN SEARCH REPORT

Application Number
EP 04 25 5015

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Y	US 5 570 683 A (ZAPOL ET AL) 5 November 1996 (1996-11-05) * column 23, line 18 - column 26, line 36 *	1,22-24	
Y	US 2004/042970 A1 (BASU SUJIT K ET AL) 4 March 2004 (2004-03-04) * example 3 *	1,22-24	
A	WO 00/62819 A (1355540 ONTARIO INC; SLUTSKY, ARTHUR; ZAMEL, NOE; WULFFHART, HAROLD) 26 October 2000 (2000-10-26) * the whole document *	1-24	
Y	PRATTER, M.R. ET AL.: "Stability of stored methacholine chloride solutions" AMERICAN REVIEW OF RESPIRATORY DISEASE, vol. 126, no. 4, 1982, pages 717-719, XP009053049 * page 717 *	25-28	
Y	WOODMAN, T. F. ET AL.: "Determination of methacholine chloride by ion-pair high-pressure liquid chromatography" JOURNAL OF LIQUID CHROMATOGRAPHY, vol. 5, no. 7, 1982, pages 1341-1348, XP009053054 * page 1344, line 7 - page 1345, line 17 *	25-28	
A	ROSENFELD, J. ET AL.: "Gas chromatographic determination of methylcholine chloride in pharmaceutical preparations" JOURNAL OF CHROMATOGRAPHY, vol. 287, 1984, pages 433-437, XP001207507 * the whole document *	25-28	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
The present search report has been drawn up for all claims			
Place of search Munich		Date of completion of the search 30 August 2005	Examiner Venturini, F
<p>CATEGORY OF CITED DOCUMENTS</p> <p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons</p> <p>& : member of the same patent family, corresponding document</p>			

5
EPO FORM 1503 03.02 (P04.001)



European Patent
Office

Application Number

EP 04 25 5015

CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing more than ten claims.

- ☐ Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims and for those claims for which claims fees have been paid, namely claim(s):
- ☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

- ☒ All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.
- ☐ As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.
- ☐ Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:
- ☐ None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:



European Patent
Office

**LACK OF UNITY OF INVENTION
SHEET B**

Application Number
EP 04 25 5015

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. claims: 1-24

formulation containing methacholine chloride in a buffer
solution having a pH between 4 and 5

2. claims: 25-28

method for determining the amount of methacholine chloride
in a sample

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 04 25 5015

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.
The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

30-08-2005

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5570683	A	05-11-1996	AT 269731 T	15-07-2004
			AU 688027 B2	05-03-1998
			AU 2205895 A	23-10-1995
			CA 2186892 A1	12-10-1995
			DE 69533190 D1	29-07-2004
			DE 69533190 T2	18-08-2005
			EP 1466641 A1	13-10-2004
			EP 0754069 A1	22-01-1997
			ES 2224123 T3	01-03-2005
			JP 9512523 T	16-12-1997
			WO 9526768 A1	12-10-1995
			AT 158509 T	15-10-1997
			AU 657726 B2	23-03-1995
			AU 9149891 A	08-07-1992
			CA 2097823 A1	06-06-1992
			DE 10299002 I1	08-05-2002
			DE 69127756 D1	30-10-1997
			DE 69127756 T2	05-02-1998
			DE 560928 T1	22-09-1994
			DE 786264 T1	02-11-2000
			DK 560928 T3	01-12-1997
			EE 3119 B1	15-10-1998
			EP 1516639 A1	23-03-2005
			EP 0560928 A1	22-09-1993
			EP 0786264 A2	30-07-1997
			ES 2082732 T1	01-04-1996
			ES 2132043 T1	16-08-1999
			GR 96300032 T1	30-06-1996
			GR 3024865 T3	30-01-1998
			GR 99300018 T1	30-06-1999
			HK 1010101 A1	23-06-2000
			JP 3510755 B2	29-03-2004
			JP 10158175 A	16-06-1998
			JP 2701978 B2	21-01-1998
			JP 6504778 T	02-06-1994
			JP 2003111845 A	15-04-2003
			LU 90886 A9	25-03-2002
			LV 12201 A ,B	20-01-1999
			NL 300081 I1	02-04-2002
			SG 47527 A1	17-04-1998
			US 5536241 A	16-07-1996
			WO 9210228 A1	25-06-1992
			US 5873359 A	23-02-1999
			US 5485827 A	23-01-1996
US 2004042970	A1	04-03-2004	AU 2003273273 A1	19-11-2004

EPO FORM P459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 04 25 5015

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

30-08-2005

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2004042970 A1		WO 2004093861 A1	04-11-2004
		AU 2003230689 A1	08-10-2003
		CA 2478974 A1	02-10-2003
		EP 1487411 A2	22-12-2004
		JP 2005520843 T	14-07-2005
		WO 03079885 A2	02-10-2003
WO 0062819 A	26-10-2000	AT 289825 T	15-03-2005
		AU 772798 B2	06-05-2004
		AU 4095500 A	02-11-2000
		WO 0062819 A1	26-10-2000
		CA 2366922 A1	26-10-2000
		DE 60018395 D1	07-04-2005
		EP 1169065 A1	09-01-2002
		JP 2002542209 T	10-12-2002
		US 6462090 B1	08-10-2002